REMARKS

Claims 1 and 5-24 are pending in the application. Claims 21-23 are withdrawn from consideration. Claims 1, 5-20 and 24 are rejected.

Interview Summary

Applicants thank Examiner Alstrum Acevedo for the courtesy of an interview on January 27, 2009. The rejections in the Final Office Action of October 14, 2008 were discussed. Applicants' representative, Barry J. Swanson, described the distinctions between the limitations of the claimed invention and the cited art. Applicant further presented evidence that the prior art did not suggest the administration of loxapine for the treatment of headaches. Solely to advance prosecution, specific limitations were discussed with respect to certain claims that are incorporated into amendments as presented in the listing of the claims.

Amendments to the Claims

Without prejudice to the Applicants' rights to present claims of equal scope in a timely filed continuing application, solely to expedite prosecution and issuance of the application, the Applicants have amended Claims 1 and 24. Applicants also have cancelled Claims 10 and 11. The amended claims and the new claims are supported by the original specification.

The amendments to the claims do not introduce new matter. The Examiner is respectfully requested to enter the amendments to the claims and allow all claims.

Claim Rejections – 35 U.S.C. § 103

The Examiner has rejected Claims 1, 5-9 and 24 under 35 U.S.C. 103(a) as being unpatentable over Burns et al. (U.S. Patent No. 5,284,133) for the reasons of record set forth on pages 3-8 of the Office Action. The Examiner has rejected Claims 10-15 under 35 U.S.C. 103(a) as being unpatentable over Burns et al. (U.S. Patent No. 5,284,133) in further view of the Drug Information Handbook, 2nd edition. The Examiner has rejected

Claims 16-17 and 19-20 under 35 U.S.C. 103(a) as being unpatentable over Burns et al. (U.S. Patent No. 5,284,133) in further view of Nguyen et al. (U.S. Patent No. 7,040,314). The Examiner has rejected claims 16-18 under 35 U.S.C. 103(a) as being unpatentable over Burns et al. (U.S. Patent No. 5,284,133) in further view of Rabinowitz et al. (US 2004/0009128). Applicants reiterate the arguments presented in the office action response submitted on July 8, 2008, and further discuss the arguments in lieu of the amendments to the Claims.

Burns et al. does not teach that loxapine hydrochloride was a known headache analgesic. To begin, the Burns reference is not about loxapine. The Examiner's cited passage reads, "For example, with neuroleptics, psychotropics, narcotic antagonists, other central nervous system (CNS) drugs and headache analgesics, such as proclorperazine, fluphenazine hydrochloride, chlorpromazine, trifluperazine hydrochloride, thioridazine hydrochloride, loxapine hydrochloride, and haloperidol decanoate, anxiolytics such as alprazolam, busiprone and diazepam; antidepressants such as amitriptyline, clomipramine, doxepine and fluoxetine; antisomnatics such as flurazepam, temazepam and trizolam; anticonvulsants such as carbemazepine, phenytoin and clorazepam; antinausea drugs such as meclizine, ..." Burns et al. Column 7, lines 12-23. The class of "neuroleptics" is the first drug class listed in the passage cited by the Examiner that includes loxapine hydrochloride. This passage does not disclose loxapine as a headache analgesic, it merely lists loxapine in its known role as an example of a neuroleptic. The Drug Information Handbook, 2nd edition, cited by the Examiner, for example, refers to loxapine's "onset of neuroleptic effect" (Drug Information Handbook, at 555;). Further, an internet search of the terms "loxapine" and "headache" illicit either Applicants' patent/application portfolio or headache as a possible side effect of loxapine when used as a neuroleptic. (Google search performed on January 24, 2009). Thus the Burns reference does not teach loxapine as a headache analgesic.

Solely to expedite prosecution of the application, Applicants have amended Claims 1 and 24 to include the limitation, "...wherein 0.3 to 6.0mg of loxapine is administered, ...". This limitation is not taught in the prior art.

With regard to dosage, the Drug Information Handbook outlines the usual dose range to be 60-100 mg/day for oral administration or 12.5-50 mg every 4-6 hours IM. The Examiner argues that the dosing range would have been apparent to a skilled artisan that the dosages required for inhalation administration would be lower than those for oral administration (DIH), because via inhalation administration the disadvantage of first-pass metabolism of the administered drug by the liver and kidneys is avoided. The AHFS Drug Information Premier Drug Information Database for the American Society of Health-system Pharmacists (see Appendix; also found at http://www.ashp.org/mngrphs/essentials/a382311e.htm ; or http://www.medscape.com/druginfo/monograph?cid=med&drugid=14375&drugname=Loxapine+Succinate+Oral&monotype=monograph&secid=3) states, "systemic bioavailability of the parent drug after oral administration of loxapine reportedly was approximately one-third that found after IM administration of an equivalent dose, which may be related to first pass metabolism." (See page 3, pharmacokinetics, absorption of the attached Appendix). Given the above discussed pharmacokinetics, the limitation of 0.3 to 6.0mg of loxapine in the amended claims is well below the dose disclosed in the Drug Information Handbook, even considering the effects of first pass metabolism. Further, the dosage from the Drug Information Handbook refers to the dosage used for a neuroleptic affect. Nothing in the prior art teaches a range of 0.3 to 6.0mg of loxapine for the treatment of headache, as loxapine was not known for its use as a headache analgesic. Thus, the prior art does not teach or suggest each and every element of Claim 1 or Claim 24. As Claims 5-9 and 12-20 depend from Claim 1, the prior art does not teach or suggest each and every element of Claims 5-9 and 12-20.

Reconsideration is respectfully requested.

Double Patenting

Claims 1, 16-17 and 19 are rejected on the ground of nonstatutory obviousness-type double patenting as unpatentable over claims 7, 9, 10, 12 and 13 of U.S. Patent No. 6,716,416.

Claims 1 and 16-19 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as unpatentable over claims 12, 15, 16 and 18 of copending Application No. 10/633,876. Claims 1 and 16-20 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as unpatentable over claims 1 and 7-9 of copending Application No. 10/633,877. Claims 1 and 5-15 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as unpatentable over claims 1 and 15 of copending Application No. 10/719,763. Claims 1 and 5-15 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1 and 15 of copending Application No. 11/346,548.

Applicants hereby agree to file appropriate terminal disclaimers in this application with respect to subject matter ultimately found to be patentable.

Conclusion

Applicants appreciate the Examiner's careful and thorough review of the application. Applicants request the Examiner to allow the application. In the event the Examiner believes a telephonic discussion would expedite allowance or help to resolve outstanding issues, prosecution of the application, then the Examiner is invited to call the undersigned.

This constitutes a request for any needed extension of time and an authorization to charge all fees therefore to Deposit Account No. 19-5117, if not otherwise specifically requested. The undersigned hereby authorizes the charge of any fees created by the filing of this document or any deficiency of fees submitted herewith to be charged to Deposit Account No. 19-5117.

Respectfully submitted,

Date: February 17, 2009

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